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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053,355	11/08/2001	Alexander B. Rossi	A-70882/RMS/AMS	5867

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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 01/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/053,355	ROSSI, ALEXANDER B.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2004* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5/20/04* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/3/04 has been entered.

The amendment and response filed 12/3/04 have been entered. Claims 37-40 have been amended, and claims 51-80 have been canceled. Claims 37-50 are pending.

In view of the amendment and the request from applicants (§ VII of the Remark), the restriction of groups II and III is now withdrawn. The linking claims will be considered to the full scope.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The prior rejection of Claims 37-39, 42-53, 56-58, 60-66 under 35 U.S.C. 103(a) as being unpatentable over *Saito et al* (J Immunol 1996;157:343-50, IDS), taken with *Zhang et al* (Chin J Biotechnol 1999;15:189-94, IDS), is withdrawn because the prior art of record does not teach or suggest to use the combination of SCF and flt-3L for expanding the CD34+ cell population or as the first step to prepare mast cells, the art of record use more than two cytokines in a combination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37-50 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 37 recites "functional" mast cells. Since the specification fails to define the term, it is unclear what the term encompasses or excludes, in another words, it is unclear what kind of mast cells are considered, "functional" or "non-functional", and thus the metes and bounds of the claims are uncertain.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Previous rejections of claims 37-39, 42-53, 56-58, 60-70, 77-80 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is withdrawn in view of the amendment.

Claims 37-50 are newly rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for generating a proliferated population of progenitor cells comprising 10^7-10^9 cells with a starting population of 10^6 CD34+ cells, and during a period of 14-16 days, does not reasonably provide enablement for generating a proliferated population of progenitor cells comprising 10^{10}-10^{11} cells with a starting population of less than 10^6, and in a period of less than 14 days. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention are summarized in *In re Wands*, (858 F2d 731, 737, 8 USPQ 2d 1400, 1404, (Fed Cir.1988)). These factors include but are not limited to the nature of the invention, the state of the prior art, the relative skill of those in the

art, the predictability of the art, the breadth of the claims, and amount of direction provided. The factors most relevant to this rejection are the scope of the claims relative to the state of the art and the levels of the skilled in the art, and whether sufficient amount of direction or guidance are provided in the specification to enable one of skill in the art to practice the claimed invention.

Given the broadest reasonable interpretation, claims 37, 46-50 encompass making a proliferated population of progenitor cells comprising 10^7-10^{11} cells with a starting cell population of between 1 to 10^5 cells and cultured for any length of time.

However, it is well known in the art of cell biology, the rate of cell growth is associated with the numbers and density of the starting cell population, and there is a limitation of the proliferative potential for a given cell even the cell is a progenitor. In view of the general knowledge in the art, *Qui et al* (J Hematother Stem Cell Res 1999;8:609-18) used a combination of SCF, flt-3L, and TPO for expansion of a CD34+ cell population, where the numbers of cells did not reach the highest level, i.e. 78 times of the original number, until day 14. In this case, the starting cell population is the same as claimed (CD34+), and the cytokine combination is similar (SCF, flt-3L, TPO). Based on the observed rates of growth, if the starting cell population is 10^6, the end cell population would be less than 10^9. Similar results could also be seen in *Zhang et al* (fig. 1, Chin J Biotechnol 1999;15:189-94, IDS) and *Schwinger et al* (Fig. 2, Ann Hematol 1999;78:364-70). Even though applicants may argue the findings show the advantage of the claimed invention, the instant specification teaches that when the starting cell population comprises 1-5 x 10^6 cells, the ending cell population contains about 2-4 x 10^9

cells (Specification, page 46, line 20-21). This figure represents about 1,000 times increases, but far short of the claimed 100,000 times increase. Accordingly, the specification does not appear to support the full scope of the invention.

Claims 37-50 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for generating cultured mast cells by contacting progenitor cells with a SCF and another cytokine, wherein the cytokine is IL-4, or IL-6, does not reasonably provide enablement for generating cultured functional mast cells by contacting said progenitors with a SCF and any other cytokine beyond IL-4 and IL-6. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Given the broadest reasonable interpretation, claim 37 encompasses contacting said progenitor cells from step a) with a SCF and any cytokine. However, the specification and art of record only teach the combination of SCF and IL-4/IL-6 for making mast cells. In view of such, the specification fails to support the full scope of the claims.

The amended claim 37 recites, "functional mast cells". Although it is unclear what kind of mast cells are considered as "functional", for the purpose of a compact prosecution, and in light of the specification, this term appears to encompass matured mast cells. However, as indicated in the previous Office actions, *Matsushima et al* (J Dermatol Sci 2000;24:4-13) teach a method that is the same as the instant step b of claim 37, and concluded that SCF and IL-6 do not promote complete maturation of

cultured human mast cells derived from UCB cells. *Matsushima et al* teach based on the electron microscopic observation, these cells are so immature that they could not distinguish MCT and MCTC based on the ultrastructural morphology (e.g abstract). To this end, the specification fails to disclose evidence contrary to the finding of *Matsushima et al*. In view of such, the invention does not appear to be enabled in the absence of clarification of the contradictory evidence found in the references.

Therefore, in view of the limited guidance, the lack of predictability of the art and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

Conclusion

No claim is allowed. Claims 37-50 appear to be free of cited prior art of record, however, they are subject to other rejections.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Ram R. Shukla** can be reached on 571-272-0735. The fax numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Q. Janice Li
Primary Examiner
Art Unit 1632

QJL
January 21, 2005